

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. – 10. (Cancelled).

11. (Currently amended) A method of making an MR imaging agent, said method comprising:

a) reacting a peptide having an N-terminal amine functional group with a linker-subunit moiety to form a modified peptide having a C-terminal amine functional group and said N-terminal amine functional group;

b) covalently attaching a linker moiety to the C-terminal amine functional group and to the N-terminal amine functional group to form a precursor MR imaging agent;

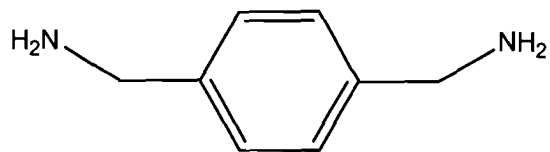
c) converting the precursor MR imaging agent to the MR imaging agent;
wherein converting the precursor MR imaging agent to the MR imaging agent comprises:

(d) reacting the precursor MR imaging agent with a precursor chelate moiety to form a covalent bond between the precursor chelate moiety and the linker moiety of the precursor MR imaging agent, ~~the precursor chelate moiety comprising a plurality of carboxylate precursor groups, the carboxylate precursor groups capable of being transformed into carboxylate moieties;~~

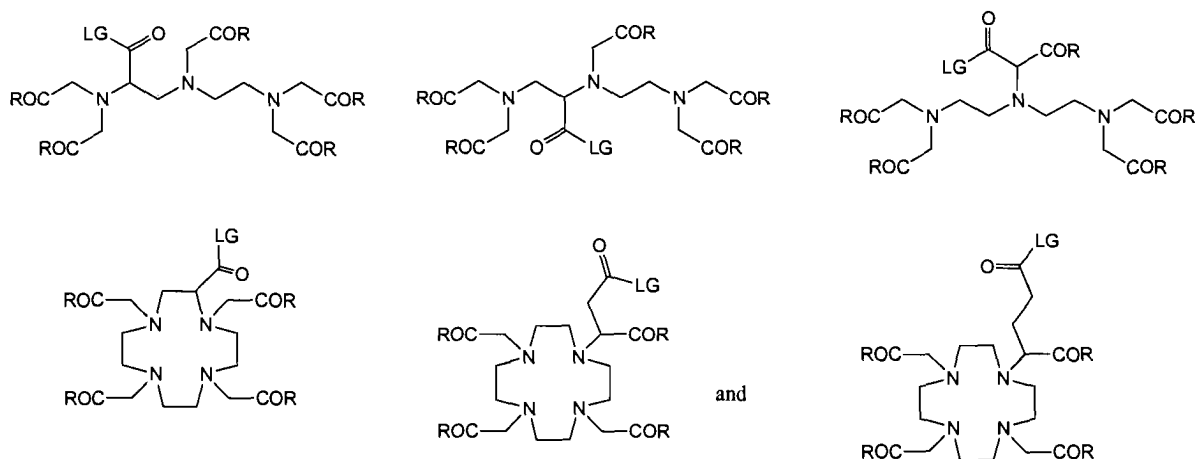
(e) reacting the covalently linked precursor MR imaging agent and precursor chelate moiety to produce transforming a plurality of the carboxylate precursor groups of the bound precursor chelate moiety to a plurality of carboxylate moieties, the carboxylate moieties capable of complexing a paramagnetic metal ion; and

(f) complexing a paramagnetic metal ion to the plurality of carboxylate moieties to produce the MR imaging agent;

wherein the linker-subunit moiety is:



wherein the precursor chelate moiety is selected from the group consisting of:



wherein LG is a leaving group selected from the group consisting of -OH, ~~activated ester~~ a pentafluorophenol (Pfp) moiety, a N-hydroxysuccinimide (NHS) moiety, a N-hydroxysulfosuccinimide salt (NHSS) moiety, a 2-thioxothiazolidin-1-yl moiety, a hydroxybenzotriazole (HBT) moiety, and a halide, and anhydride, and wherein each R, independently, is an O⁻ or an O⁻ precursor selected from the group consisting of OH, -O-Me, O-Et, O-tBu, O-benzyl, and O-allyl, ~~so that R, upon conversion to O⁻, is capable of forming a carboxylate moiety with its adjacent carbonyl.~~

12. – 13. (Cancelled).

14. (Currently amended) A method of making an MR imaging agent, said method comprising:

a) reacting a peptide having an N-terminal amine functional group with a linker-subunit moiety to form a modified peptide having a C-terminal amine functional group and said N-terminal amine functional group;

b) covalently attaching a linker moiety to the C-terminal amine functional group and to the N-terminal amine functional group to form a precursor MR imaging agent;

c) converting the precursor MR imaging agent to the MR imaging agent;

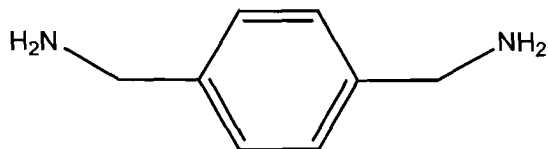
wherein converting the precursor MR imaging agent to the MR imaging agent comprises:

(d) reacting the precursor MR imaging agent with a precursor chelate moiety to form a covalent bond between the precursor chelate moiety and the linker moiety of the precursor MR imaging agent, ~~the precursor chelate moiety comprising a plurality of carboxylate precursor groups, the carboxylate precursor groups capable of being transformed into carboxylate moieties;~~

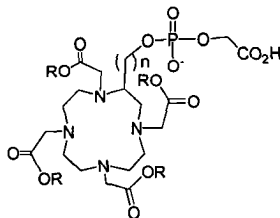
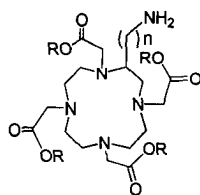
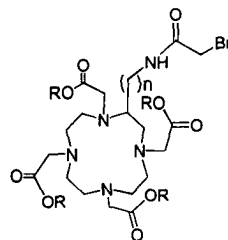
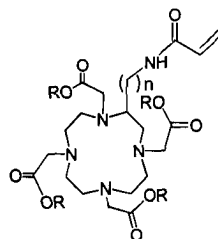
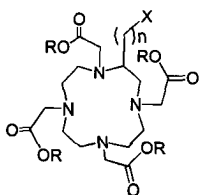
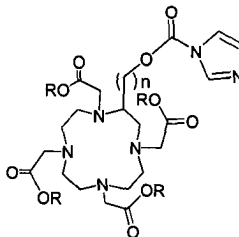
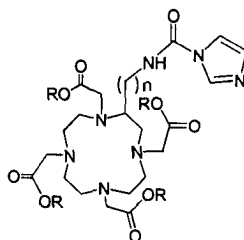
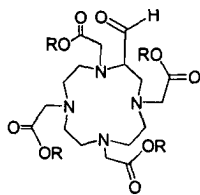
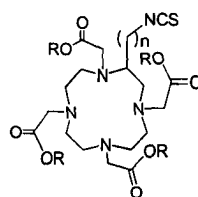
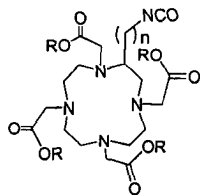
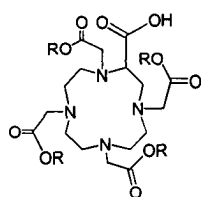
(e) reacting the covalently linked precursor MR imaging agent and precursor chelate moiety to produce ~~transforming a plurality of the carboxylate precursor groups of the bound precursor chelate moiety to a plurality of carboxylate moieties, the carboxylate moieties capable of complexing a paramagnetic metal ion; and~~

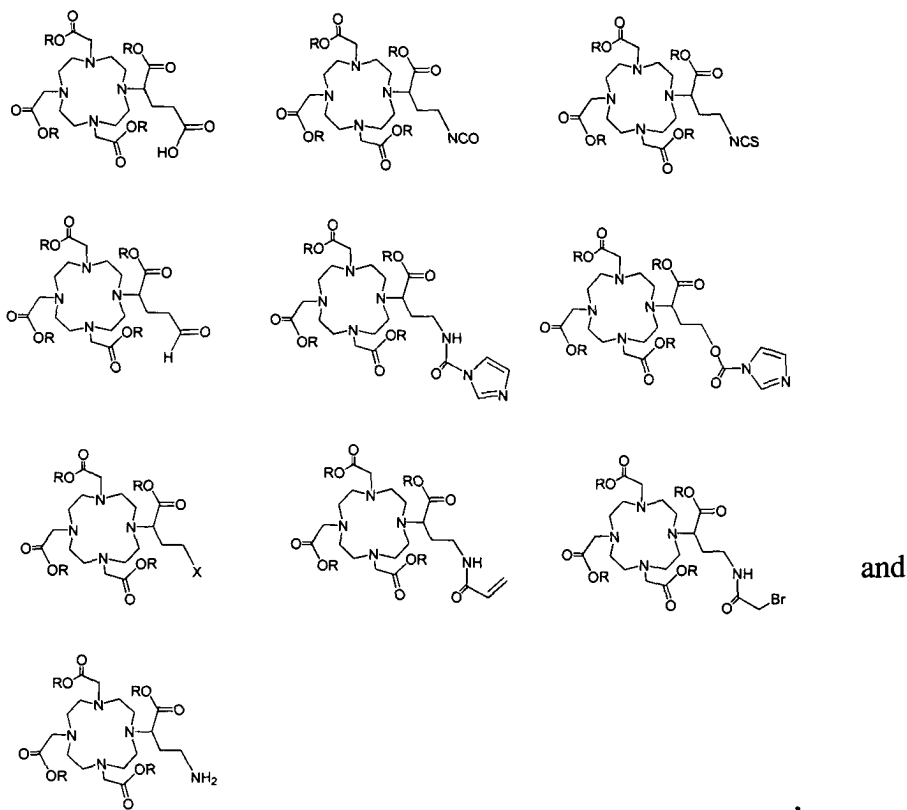
(f) complexing a paramagnetic metal ion to the plurality of carboxylate moieties to produce the MR imaging agent;

wherein the linker-subunit moiety is:



wherein the precursor chelate moiety is selected from the group consisting of:





wherein:

n is an integer from 1 to 4;

R is selected from the group consisting of a negative charge and a negative charge precursor ~~capable of being transformed into a negative charge~~; and

X is a chemical leaving group selected from the group consisting of -Cl, -Br, -I, -MsO, -TsO, and -TfO; and

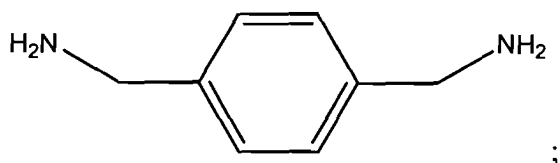
wherein the negative charge precursor is selected from the group consisting of -H, -Me, -Et, -t-Bu, -benzyl, and -allyl.

15. (Cancelled).

16. (Currently amended) A method of making an MR imaging agent, said method comprising:

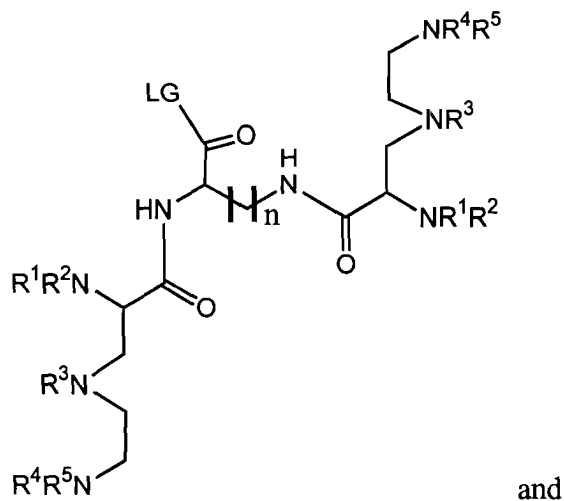
- a) reacting a peptide having an N-terminal amine functional group with a linker-subunit moiety to form a modified peptide having a C-terminal amine functional group and said N-terminal amine functional group;
- b) covalently attaching a linker moiety to the C-terminal amine functional group and to the N-terminal amine functional group to form a precursor MR imaging agent; and
- c) converting the precursor MR imaging agent to the MR imaging agent;

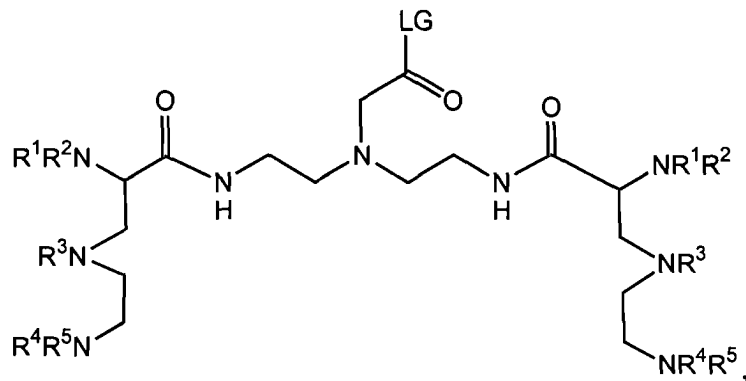
wherein the linker-subunit moiety is:



wherein the linker moiety ~~is~~ has been covalently conjugated to a precursor chelate moiety, ~~the to form a covalent conjugate comprising a plurality of carboxylate precursor groups, the carboxylate precursor groups capable of being transformed into carboxylate moieties;~~

wherein the covalent conjugate of the linker moiety and the precursor chelate moiety is selected from the group consisting of





wherein n is an integer from 1 to 4;

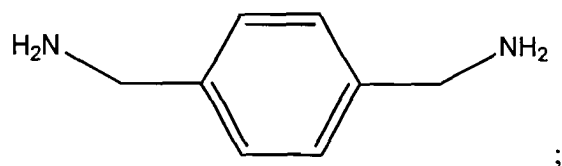
LG is a leaving group selected from the group consisting of -OH, ~~activated ester~~ a pentafluorophenol (Pfp) moiety, a N-hydroxysuccinimide (NHS) moiety, a N-hydroxysulfosuccinimide salt (NHSS) moiety, a 2-thioxothiazolidin-1-yl moiety, a hydroxybenzotriazole (HBT) moiety, and a halide, ~~and anhydride~~; and

R¹, R², R³, R⁴, and R⁵ are independently selected from the group consisting of an acetate moiety, a -Me, -Et, or -t-Bu protected acetate moiety, an acetamide moiety, and an acetoxy moiety.

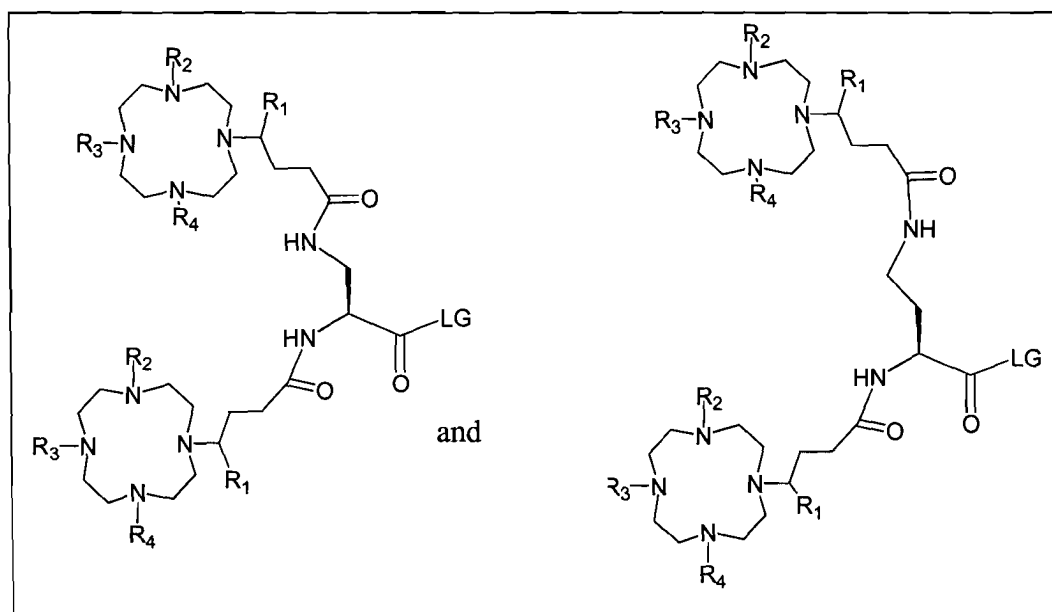
17. (Currently amended) A method of making an MR imaging agent, said method comprising:

- a) reacting a peptide having an N-terminal amine functional group with a linker-subunit moiety to form a modified peptide having a C-terminal amine functional group and said N-terminal amine functional group;
- b) covalently attaching a linker moiety to the C-terminal amine functional group and to the N-terminal amine functional group to form a precursor MR imaging agent; and
- c) converting the precursor MR imaging agent to the MR imaging agent;

wherein the linker-subunit moiety is:



wherein the linker moiety is moiety ~~is~~ has been covalently conjugated to a precursor chelate moiety, ~~the to form a covalent conjugate comprising a plurality of carboxylate precursor groups, the carboxylate precursor groups capable of being transformed into carboxylate moieties;~~ wherein the covalent conjugate of the linker moiety and the precursor chelate moiety is selected from the group consisting of:



wherein:

LG is a leaving group selected from the group consisting of -OH, ~~activated ester~~ a pentafluorophenol (Pfp) moiety, a N-hydroxysuccinimide (NHS) moiety, a N-hydroxysulfosuccinimide salt (NHSS) moiety, a 2-thioxothiazolidin-1-yl moiety, a hydroxybenzotriazole (HBT) moiety, and a halide, ~~and anhydride;~~ and

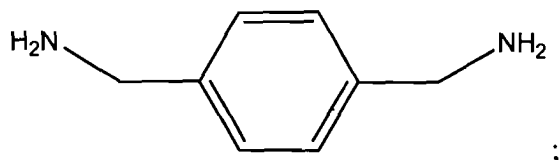
R^1 , R^2 , R^3 , and R^4 are selected from the group consisting of an acetate moiety, a -Me, -Et, or -t-Bu protected acetate moiety, an acetamide moiety, and an acetoxy moiety.

18. (Cancelled).

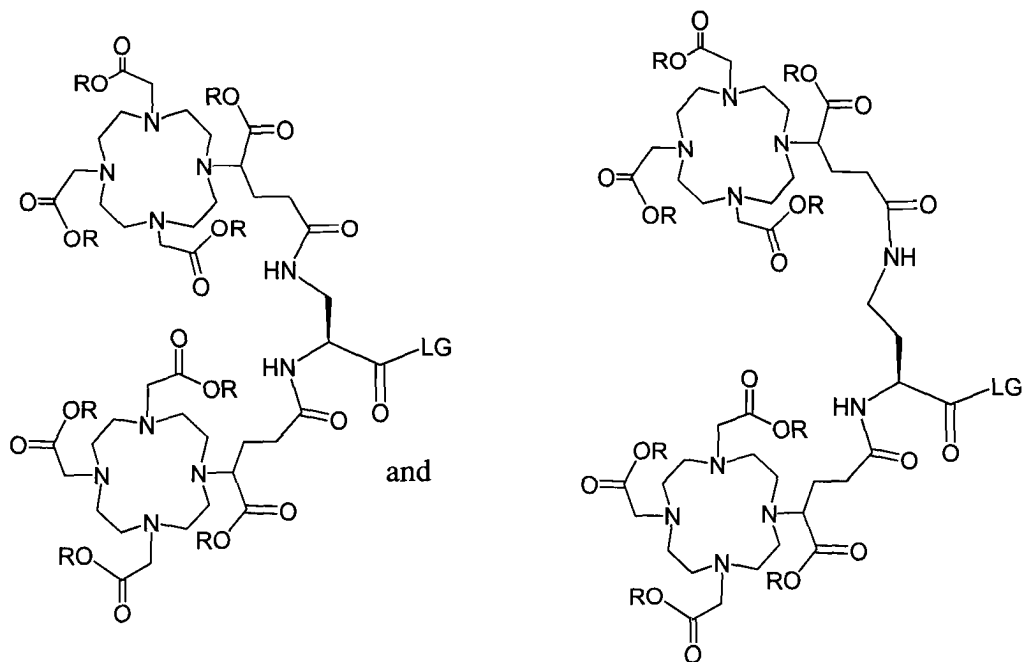
19. (Currently amended) A method of making an MR imaging agent, said method comprising:

- a) reacting a peptide having an N-terminal amine functional group with a linker-subunit moiety to form a modified peptide having a C-terminal amine functional group and said N-terminal amine functional group;
- b) covalently attaching a linker moiety to the C-terminal amine functional group and to the N-terminal amine functional group to form a precursor MR imaging agent; and
- c) converting the precursor MR imaging agent to the MR imaging agent;

wherein the linker-subunit moiety is:



wherein the linker moiety is has been covalently conjugated to a precursor chelate moiety, ~~the to form a covalent conjugate comprising a plurality of carboxylate precursor groups, the carboxylate precursor groups capable of being transformed into carboxylate moieties;~~
wherein the covalent conjugate of the linker moiety and the precursor chelate moiety is selected from the group consisting of:



wherein:

R is a -tBu group,

LG is a leaving group selected from the group consisting of -OH, ~~activated ester~~ a pentafluorophenol (Pfp) moiety, a N-hydroxysuccinimide (NHS) moiety, a N-hydroxysulfosuccinimide salt (NHSS) moiety, a 2-thioxothiazolidin-1-yl moiety, a hydroxybenzotriazole (HBT) moiety, and a halide, ~~and anhydride~~.

20. (Cancelled).

21. (Previously Presented) The method of claim 11 or 14, wherein the paramagnetic metal ion is selected from the group consisting of: Gd(III), Fe(III), Mn(II and III), Cr(III), Cu(II), Dy(III), Tb(III and IV), Ho(III), Er(III), Pr(III), Eu(II) and Eu(III).

22. (Original) The method of claim 21, wherein the paramagnetic metal ion is Gd(III).

23. - 77. (Cancelled).